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REMARKS

Amendment to claim 1

Applicants request entry of the amendments to claims 1, 3, 6, 12 and 13. The amendment to claim 1 is in accordance with the Examiner's comments in the Final Office Action dated July 28, 2003 regarding rejections under 35 U.S.C. § 112, first paragraph, enablement and written description of naturally occurring variants that are "90% identical to the full length of the sequence of SEQ ID NO:3" and removes issues for appeal. The amendments to claims 3 and 6 are in accordance with the Examiner's comments on page 2 of the Final Office Action requesting Applicants to delete the non-elected embodiments from the claims in the interest of facilitating the prosecution of this application. The amendments to claims 12 and 13 (currently withdrawn by the Examiner) are intended to place these claims in proper form for allowance upon rejoinder. Therefore, it is believed that entry of this Amendment is proper.

Applicants expressly state that these claims are not being amended for reasons related to patentability, and are in fact fully supported by the specification as filed. Applicants expressly reserve the right to reinstate these claims or to add other claims during prosecution of this application or a continuation or divisional application. Applicants expressly do not disclaim the subject matter of any invention disclosed in the specification which is not set forth in the instantly amended claims. Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

Rejoinder of Method Claims

Applicants reiterate that upon allowance of any product claim, there should be rejoinder of "method of use" claims 12-13, in accordance with the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)."

Rejections under 35 U.S.C. § 112, first paragraph, Enablement

Claims 1-2 and 9-11 were rejected under 35 U.S.C. § 112, first paragraph "because the specification, while being enabling for an antibody to the full length polypeptide of SEQ ID NO:3 or an immunogenic fragment thereof; does not reasonably provide enablement for an antibody to a polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the full length of the sequence of SEQ ID NO:3" wherein said naturally-occurring amino acid sequence supports NADH dehydrogenase activity." (Final Office Action at page 2.)

The Amendment to claim 1 removes the recitation of "a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the full length of the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:7, wherein said naturally-occurring amino acid sequence supports NADH dehydrogenase activity" and, therefore, removes the basis for the rejection under 35 U.S.C. § 112, first paragraph, with respect to enablement. Accordingly, it is respectfully requested that this rejection be withdrawn.

Applicants expressly state that this claim is not being amended for reasons related to patentability, and is in fact fully supported by the specification as filed. Applicants expressly reserve the right to reinstate this claim or to add other claims during prosecution of this application or a continuation or divisional application. Applicants expressly do not disclaim the subject matter of any invention disclosed in the specification which is not set forth in the instantly amended claims. Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

Rejections under 35 U.S.C. § 112, first paragraph, Written Description

Claims 1-2 and 9-11 were rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner alleges that:

- a polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the full length of the sequence of SEQ ID NO:3" wherein said naturally-occurring amino acid sequence supports NADH dehydrogenase activity is a recitation of a genus of polypeptides for

which Applicant has disclosed a single species: the polypeptide of SEQ ID NO:3. (Final Office Action at page 4.)

- Applicant does not appear to have been in possession of the genus of polypeptides to which the instantly recited antibody specifically binds. Thus the Examiner maintains that Applicant in turn does not appear to be in possession of the genus of antibodies specifically binding these polypeptides. (Final Office Action at page 4.)

The Amendment to claim 1 removes the recitation of "a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the full length of the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:7, wherein said naturally-occurring amino acid sequence supports NADH dehydrogenase activity" and, therefore, removes the basis for the rejection under 35 U.S.C. § 112, first paragraph, with respect to the written description. Accordingly, it is respectfully requested that this rejection be withdrawn.

Applicants expressly state that this claim is not being amended for reasons related to patentability, and is in fact fully supported by the specification as filed. Applicants expressly reserve the right to reinstate this claim or to add other claims during prosecution of this application or a continuation or divisional application. Applicants expressly do not disclaim the subject matter of any invention disclosed in the specification which is not set forth in the instantly amended claims. Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

Prior Art Rejections under 35 U.S.C. § 102(b)

Claims 1 and 4 were rejected under 35 U.S.C. § 102(b) as being anticipated by Bentlage et al. (Biochimica Biophysica Acta, 1234:63-73, 1995; of record). The basis for this rejection appears to be the Examiner's opinion that, although the polypeptide sequence of SEQ ID NO:3 is not explicitly disclosed in Bentlage et al., "*SEQ ID NO:3 would be an inherent property of the polypeptide recognized* [by the antibody disclosed in Bentlage et al.]." (Final Office Action at page 5, emphasis in original.) In making this rejection the Examiner takes the position that "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' [*sic*] under 35 U.S.C.

102, on prima facie obviousness' [*sic*] under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...In re Fitzgerald, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)). (See MPEP 2112 and 2112.01)." (Final Office Action at page 6.) Applicants respectfully submit that not only is the Examiner's analysis of the requirements for inherency incorrect, but the Examiner's application of the case law provided by *In re Fitzgerald* and *In re Best* is premature since ***this may only be applied after the Examiner has provided evidence showing inherency***. (See MPEP 2112.)

The requirements for making a rejection based on inherency are well established by case law:

> The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). [Emphasis in original.]

> To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. ***Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.***' *In re Robertson,* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted). [Emphasis added.]

> In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). [Emphasis in original.]

The Examiner has not provided any evidence or sound technical reasoning that would support the theory of inherency as the basis for making this rejection under 35 U.S.C. § 102(b). The Examiner has admitted that "the polypeptide of 15kD recognized by the antibodies [of Bentlage et al.] was not shown to comprise SEQ ID NO:3" (Final Office Action at page 5). Yet the Examiner insists that SEQ ID NO:3 would be an inherent property of the polypeptide recognized. This position is legally unsupportable. (See *In re Rijckaert*, *In re Oelrich*, *In re Robertson,* and *Ex parte Levy*, *supra.*)

The Examiner does not deny that post filing date evidence indicates that there are a total of 7 nuclear-encoded polypeptide subunits in human Complex I that have a similar size to the polypeptide of SEQ ID NO:3. Nonetheless, the Examiner asserts that since the antibodies of Bentlage et al. are in the form of an antisera and there are many different individual antibodies in an antisera preparation, nothing precludes the antisera of Bentlage et al. containing antibodies to each of the polypeptides in human Complex I. Applicants respectfully submit that there is no evidence that the antisera of Bentlage et al. is known to contain antibodies which ***specifically bind*** to the polypeptide sequence of SEQ ID NO:3. Because the Examiner has failed to provide any *prima facie* evidence that the antisera of Bentlage et al. includes "an isolated antibody that specifically binds...the polypeptide of SEQ ID NO:3...," as recited in claim 1, the rejection under 35 U.S.C. § 102(b) based on inherency is not legally supportable. ('...Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' *In re Robertson, supra.*) Accordingly, the teachings of Bentlage et al. cannot anticipate the instant claims.

Even if it were to be the case that the antisera of Bentlage et al. contained antibodies that somehow bound to the polypeptide of SEQ ID NO:3, the present invention would still not be anticipated by the prior art. The present claims recite an antibody which ***specifically binds*** to a polypeptide comprising, *inter alia*, the amino acid sequence of SEQ ID NO:3. Thus, the antibody encompassed by the claims binds the recited polypeptides, and not other polypeptides.

The Specification teaches that the antibodies of claims 1 and 4 ***specifically bind*** to a polypeptide of SEQ ID NO:3. "Specific binding" or "specifically binding" is defined in the specification at page 10, lines 1-7:

> The terms "specific binding" or "specifically binding", as used herein, in reference to the interaction of an antibody and a protein or peptide, mean that the interaction is dependent upon the presence of a particular structure (i.e., the antigenic determinant or epitope) on the protein; in other words, the antibody is recognizing and binding to a specific protein structure rather than to proteins in general. For example, if an antibody is specific for epitope "A", the presence of a protein containing epitope A (or free, unlabeled A) in a reaction containing labeled "A" and the antibody will reduce the amount of labeled A bound to the antibody.

The words of a claim must be given their "plain meaning" unless applicant has provided a clear definition in the specification (MPEP §2111.01). One of ordinary skill in the art would interpret claims 1 and 4 to mean that the claimed antibody and its interaction with a particular structure leads to "recognizing and binding to a specific protein structure rather than to proteins in general," i.e., the polypeptide of SEQ ID NO:3. Applicants can be their own lexicographer. Therefore, Applicants' use of a term is determined by the Applicants and does not require the use to be consistent "with the well-known and art-recognized specificity of antibody interaction with epitopes" as the Examiner would require (Office Action of March 21, 2002, page 5).

The Office Action of March 21, 2002 further alleges that Applicants disregard the art recognized use of the term "polyclonal antibody" to "inherently comprise a mixture of many different individual antibodies elicited by the immunizing antigen" (page 6). Bentlage et al. teach the use of a bovine polyclonal antibody produced in response to exposure to bovine multi-polypeptide Complex I antigen, a holo-enzyme. The bovine Complex I antibody is also taught by Bentlage et al. to bind to about 10 human Complex I subunits. The Office Action concludes (incorrectly) that Bentlage et al. teach a bovine polyclonal antibody that binds a 15 kD protein of human Complex I and therefore anticipates claims 1 and 4 (Office Action of March 21, 2002, page 6).

The antibodies of claims 1 and 4 are to a single polypeptide comprising the amino acid sequence of SEQ ID NO:3, not a multi-polypeptide composition. Applicants' NDS2 protein (SEQ ID NO:3) is taught in the specification to have chemical and structural homology with the bovine B15 subunit, one of several nuclear encoded NADH-D subunits (Specification, page 12 lines 27-31). Applicants' identification of SEQ ID NO:3 as a homolog of a nuclear encoded NADH-D subunit would strongly suggest to one of ordinary skill in the art that SEQ ID NO:3 is also a nuclear encoded subunit of NADH-D.

Upon closer examination of some 32 nuclear-encoded human Complex I protein subunits, there are at least three subunits of comparable amino acid sequence length as SEQ ID NO:3:

Subunit	Length	GenBank Accession No.
NDUFB6	128 amino acids in length	AF035840
NDUFS6	124 amino acids in length	AF044959
NDUFB4	129 amino acids in length	AF044957 (length of SEQ ID NO:3)
NDUFA6	128 amino acids in length	AF047182

(Loeffen et al. Biochem. Biophys. Res. Comm. (1998) 253:415-422, p. 416, of record).

The Examiner alleges that the results of Figure 4a in the Bentlage et al. paper are such that "the ordinary artisan would have had a reasonable expectation that antibodies produced would have specifically bound the polypeptide of SEQ ID NO:3" (Office Action of March 21, 2002, p. 7). Figure 4a neither identifies which subunits the arrows are designating in the myopathy patients tested, nor exhibits the results. Moreover, as taught by Bentlage et al., bovine polyclonal antibodies against purified beef heart Complex I react with only approximately 15 subunits of the enzyme in human mitochondria as well as a generalized reduction of all cross-reacting polypeptides in skeletal mitochondrial proteins from myopathy patients. Additionally, the bovine Complex I polyclonal antibody did not detect mitochondrial encoded (ND) subunits and, in fact, detected only nuclear encoded subunits (Bentlage et al. p. 63). At the time the Bentlage paper was published, the human Complex I enzyme subunits consisting of NDUFA3, -7, -10, NDUFB2, -4, -8, -10 and NDUFC2 had not yet been sequenced (Loeffen et al. p. 416). Therefore, what is readily apparent to one of skill in the art upon examination of Figure 4a is that it is impossible to determine which, if any, of the four subunits described by Loeffen et al. were actually detected, let alone that the bovine polyclonal antibody had specifically bound SEQ ID NO:3. Therefore, the polyclonal antibody of bovine Complex I can neither be anticipated to specifically bind SEQ ID NO:3, nor provide to one of skill in the art the expectation that such binding would even occur. Therefore, claims 1 and 4 are not anticipated by the teachings of Bentlage et al.

For at least the reasons stated above, Applicants respectfully request that this rejection be withdrawn.

Prior Art Rejections under 35 U.S.C. § 103(a)

Claims 1 and 4 stand rejected under 35 U.S.C. § 103(a) for alleged obviousness over Walker et al. (J. Mol. Bio. 1992; 226:1051-1072; of record) in view of Bentlage et al. (Biochimica Biophysica Acta 1995; 1234:63-73) and in further view of Ramakrishnan et al. (US Pat No. 5,817,310; of record). As has been submitted in the preceding discussion regarding the anticipation rejections under 35 U.S.C. §102(b), claims 1 and 4 are not anticipated by Bentlage et al.

Bentlage et al. relates to a study of ***mitochondrial*** DNA-encoded (not nuclear encoded) subunits of human respiratory chain NADH dehydrogenase (Complex I) via the use of various antibodies. Those antibodies included polyclonal antibodies raised against the mtDNA-encoded ND4, ND5 and ND6 subunits. The ND4, ND5 and ND6 subunits have no apparent similarity to SEQ ID NO:3 of the present invention, and none has been asserted by the Examiner (See Clustal W alignments of SEQ ID NO:3 with the polypeptide sequences used to generate antibodies to the mtDNA-encoded ND4, ND5 and ND6 subunits, Attachment 1).

Rather, the Examiner appears to rely on the description in Bentlage et al. at page 65, section 2.4, of a polyclonal antibody raised against the bovine Complex I holo-enzyme. In this regard, the Office Action points to Figure 4a of Bentlage et al. as showing "a polyclonal antibody that binds a 15kD protein of human Complex I" (Office Action of May 7, 2001 at page 8). Bentlage et al., however, shows that this antibody does not specifically bind to a 15 kD protein. That is, the Western blot in panel A of Figure 4 shows that the antibody against bovine Complex I holo-enzyme binds to multiple subunits of the human complex. See also page 65, section 2.4 of Bentlage et al., which states that the antibodies against the bovine Complex I holo-enzyme "showed a reaction with approximately 10 subunits of Complex I preparation from bovine and human heart tissue." It is also notable that the Examiner states that "the polypeptide of 15kD recognized by the antibodies was not shown to comprise SEQ ID NO:3" (Office Action of May 7, 2001 at page 8). Furthermore, one of skill in the art would not expect that any of the antibodies disclosed in Bentlage et al. that were raised against ***mitochondrial*** DNA-encoded (not nuclear encoded) subunits of human respiratory chain NADH

dehydrogenase (Complex I) would ***specifically bind*** to Applicants' nuclear encoded subunit of NADH-D (SEQ ID NO:3). Clearly, then, Bentlage et al. does not disclose an antibody which specifically binds SEQ ID NO:3.

Walker et al. does not make up for the deficiencies of Bentlage et al. Walker et al. describe a bovine B15 sequence of NADH:ubiquinone oxidoreductase which has some sequence similarity to SEQ ID NO:3. Again, the Examiner relies on the previously discussed limitation of "specifically binds" to assert that the polypeptide taught by Walker et al. which allegedly has "numerous shared epitopes" with SEQ ID NO:3 would therefore, also "specifically bind" to the claimed antibody. The Office Action provides no evidence of what "shared epitopes" exist between SEQ ID NO:3 and the B15 polypeptide of Walker et al. Walker et al. do not teach epitopes of bovine B15. The B15 polypeptide of Walker et al. is alleged by the Examiner to have 75.8% identity with SEQ ID NO:3, and would be understood by one of skill in the art to also have about 24% nonidentity to SEQ ID NO:3. The claimed invention recites an isolated antibody which specifically binds to a polypeptide that is, *inter alia*, the full length polypeptide of SEQ ID NO:3 or an immunogenic fragment thereof. Clearly, the sequence taught by Walker et al. is neither "a polypeptide comprising the amino acid sequence of...SEQ ID NO:3" nor is it "an immunogenic fragment of a polypeptide consisting of at least 10 contiguous amino acid residues of an amino acid sequence...of...SEQ ID NO:3..." as recited in claim 1. Therefore, the sequence taught by Walker et al. is not encompassed by the claimed invention.

Ramakrishnan et al. describes various methods for producing antibodies, but has no information at all relating to SEQ ID NO:3. Hence, that document would not have guided one of skill in the art to the claimed subject matter.

Taken together, the teachings of Bentlage et al., Walker et al. and Ramakrishnan et al. do not provide a *prima facie* case for obviousness for the claimed invention and do not support a rejection for obviousness under 35 U.S.C. § 103(a).

For at least the reasons stated above, it is respectfully requested that this rejection be withdrawn.

Request for Examiner Interview

Applicants hereby request an appointment for a telephone interview with the Primary Patent Examiner as well as the Supervisory Patent Examiner prior to any further action on this application. The purpose of the telephone interview is to clarify the issues discussed above as well as to expedite the further prosecution of this patent application. Applicants request that the Patent Examiner propose a date and time during which the Interview may take place.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (650) 855-0555.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,
INCYTE CORPORATION

Date: 23 December 2003

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Enclosure:

1. CLUSTALW alignments of SEQ ID NO:3 with the polypeptide sequences (from Table 1 of Bentlage et al.) used to generate antibodies to the mtDNA-encoded ND4, ND5 and ND6 subunits (9 pages).

PF-0187-2 DIV
Attachment 1
USSN: 09/726,899

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☐ 1600202CD1
☐ ND4-I1_(81-94)

CLUSTAL W (1.7) Multiple Sequence Alignments

```
Sequence format is Pearson
Sequence 1: 1600202CD1          129 aa
Sequence 2: ND4-I1__81-94_       14 aa
Start of Pairwise alignments
Aligning...
Sequences (1:2) Aligned. Score:  28
Start of Multiple Alignment
There are 1 groups
Aligning...
Group 1:                    Delayed
Sequence:1     Score:0
Sequence:2     Score:109
Alignment Score -1
CLUSTAL-Alignment file created  [baatXaWNV.aln]
CLUSTAL W (1.7) multiple sequence alignment


1600202CD1          MSFPKYKPSSLRTLPETLDPAEYNISPETRRAQAERLAIRAQLKREYLLQYNDPNRRGLI
ND4-I1__81-94_      ----------------------------------ZRHLSSEPLSRKKL------------
                                                      *      *.*: *

1600202CD1          ENPALLRWAYARTINVYPNFRPTPKNSLMGALCGFGPLIFIYYIIKTERDRKEKLIQEGK
ND4-I1__81-94_      ------------------------------------------------------------

1600202CD1          LDRTFHLSY
ND4-I1__81-94_      ---------
```

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- ☐ 1600202CD1
- ☐ ND4-I2_(135-145)

```
 CLUSTAL W (1.7) Multiple Sequence Alignments


Sequence format is Pearson
Sequence 1: 1600202CD1            129 aa
Sequence 2: ND4-I2__135-145_       11 aa
Start of Pairwise alignments
Aligning...
Sequences (1:2) Aligned. Score:  18
Start of Multiple Alignment
There are 1 groups
Aligning...
Group 1:                    Delayed
Sequence:1     Score:0
Sequence:2     Score:86
Alignment Score -2
CLUSTAL-Alignment file created  [baanBaOYV.aln]
CLUSTAL W (1.7) multiple sequence alignment


1600202CD1            MSFPKYKPSSLRTLPETLDPAEYNISPETRRAQAERLAIRAQLKREYLLQYNDPNRRGLI
ND4-I2__135-145_      ----------------------RWGNQPERLNA---------------------------
                                           .:. .**  .*

1600202CD1            ENPALLRWAYARTINVYPNFRPTPKNSLMGALCGFGPLIFIYYIIKTERDRKEKLIQEGK
ND4-I2__135-145_      ------------------------------------------------------------


1600202CD1            LDRTFHLSY
ND4-I2__135-145_      ---------
```

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- ☐ 1600202CD1
- ☐ ND4-I3_(277-285)

CLUSTAL W (1.7) Multiple Sequence Alignments

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Sequence 2: ND4-I3__277-285_        9 aa
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Aligning...
Sequences (1:2) Aligned. Score:  44
Start of Multiple Alignment
There are 1 groups
Aligning...
Group 1: Sequences:   2      Score:76
Alignment Score -3
CLUSTAL-Alignment file created  [baajJa43V.aln]
CLUSTAL W (1.7) multiple sequence alignment

1600202CD1            MSFPKYKPSSLRTLPETLDPAEYNISPETRRAQAERLAIRAQLKREYLLQYNDPNRRGLI
ND4-I3__277-285_      ------------------------------------------------------------

1600202CD1            ENPALLRWAYARTINVYPNFRPTPKNSLMGALCGFGPLIFIYYIIKTERDRKEKLIQEGK
ND4-I3__277-285_      -------------------LRQTDLKSL--------------------------------
                                         :* *  :**

1600202CD1            LDRTFHLSY
ND4-I3__277-285_      ---------
```

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- ☐ 1600202CD1
- ☐ ND4-I4_(329-339)

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 CLUSTAL W (1.7) Multiple Sequence Alignments


Sequence format is Pearson
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Sequence 2: ND4-I4__329-339_       11 aa
Start of Pairwise alignments
Aligning...
Sequences (1:2) Aligned. Score:  27
Start of Multiple Alignment
There are 1 groups
Aligning...
Group 1:                    Delayed
Sequence:1     Score:0
Sequence:2     Score:85
Alignment Score -4
CLUSTAL-Alignment file created  [baaO1aG7V.aln]
CLUSTAL W (1.7) multiple sequence alignment


1600202CD1            MSFPKYKPSSLRTLPETLDPAEYNISPETRRAQAERLAIRAQLKREYLLQYNDPNRRGLI
ND4-I4__329-339_      ------------------------------------------------------------


1600202CD1            ENPALLRWAYARTINVYPNFRPTPKNSLMGALCGFGPLIFIYYIIKTERDRKEKLIQEGK
ND4-I4__329-339_      ----LANSNYERTHS---------------------------------------------
                          * .  * ** .

1600202CD1            LDRTFHLSY
ND4-I4__329-339_      ---------
```

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- ☐ 1600202CD1
- ☐ ND4-I5_(420-435)

CLUSTAL W (1.7) Multiple Sequence Alignments

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Sequence 2: ND4-I5__420-435_       16 aa
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Aligning...
Sequences (1:2) Aligned. Score:  18
Start of Multiple Alignment
There are 1 groups
Aligning...
Group 1:                    Delayed
Sequence:1     Score:0
Sequence:2     Score:112
Alignment Score -8
CLUSTAL-Alignment file created  [baa4UaOaW.aln]
CLUSTAL W (1.7) multiple sequence alignment


1600202CD1            MSFPKYKPSSLRTLPETLDPAEYNISPETRRAQAERLAIRAQLKREYLLQYNDPNRRGLI
ND4-I5__420-435_      ------------------------------------------------------------


1600202CD1            ENPALLRWAYARTINVYPNFRPTPKNSLMGALCGFGPLIFIYYIIKTERDRKEKLIQEGK
ND4-I5__420-435_      ---------THHINNMLPSFTRENT-----------------------------------
                                 :  *: *.*    .

1600202CD1            LDRTFHLSY
ND4-I5__420-435_      ---------
```

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Retrieval | BLAST2 | FASTA | ClustalW | GCG Assembly | Phrap | Translation

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- ☐ 1600202CD1
- ☐ ND4-C_(451-459)

CLUSTAL W (1.7) Multiple Sequence Alignments

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Sequence format is Pearson
Sequence 1: 1600202CD1           129 aa
Sequence 2: ND4-C__451-459_        9 aa
Start of Pairwise alignments
Aligning...
Sequences (1:2) Aligned. Score:  22
Start of Multiple Alignment
There are 1 groups
Aligning...
Group 1:                    Delayed
Sequence:1     Score:0
Sequence:2     Score:66
Alignment Score -9
CLUSTAL-Alignment file created  [baaqUaGeW.aln]
CLUSTAL W (1.7) multiple sequence alignment


1600202CD1           MSFPKYKPSSLRTLPETLDPAEYNISPETRRAQAERLAIRAQLKREYLLQYNDPNRRGLI
ND4-C__451-459_      ------------------------------------------------------------


1600202CD1           ENPALLRWAYARTINVYPNFRPTPKNSLMGALCGFGPLIFIYYIIKTERDRKEKLIQEGK
ND4-C__451-459_      ----------------------------PDIITGFSS----------------------
                                                 . : **..

1600202CD1           LDRTFHLSY
ND4-C__451-459_      ---------
```

Submit sequences to: BLAST2 Submit Reset

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ClustalW Results

Sequences | Help

Retrieval | BLAST2 | FASTA | ClustalW | GCG Assembly | Phrap | Translation

 SeqServer Version 4.6 Jan 2002

☐ 1600202CD1
☐ ND4-C_(451-459)

```
 CLUSTAL W (1.7) Multiple Sequence Alignments


Sequence format is Pearson
Sequence 1: 1600202CD1          129 aa
Sequence 2: ND4-C__451-459_       9 aa
Start of Pairwise alignments
Aligning...
Sequences (1:2) Aligned. Score:  22
Start of Multiple Alignment
There are 1 groups
Aligning...
Group 1:                    Delayed
Sequence:1     Score:0
Sequence:2     Score:66
Alignment Score -9
CLUSTAL-Alignment file created  [baa6ca4iW.aln]
CLUSTAL W (1.7) multiple sequence alignment


1600202CD1           MSFPKYKPSSLRTLPETLDPAEYNISPETRRAQAERLAIRAQLKREYLLQYNDPNRRGLI
ND4-C__451-459_      ------------------------------------------------------------


1600202CD1           ENPALLRWAYARTINVYPNFRPTPKNSLMGALCGFGPLIFIYYIIKTERDRKEKLIQEGK
ND4-C__451-459_      ----------------------------PDIITGFSS----------------------
                                                 . : **..

1600202CD1           LDRTFHLSY
ND4-C__451-459_      ---------
```

Submit sequences to: BLAST2 Submit Reset

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ClustalW Results

Sequences | Help

Retrieval | BLAST2 | FASTA | ClustalW | GCG Assembly | Phrap | Translation

 SeqServer Version 4.6 Jan 2002

- ☐ 1600202CD1
- ☐ ND5-I_(21-35)

CLUSTAL W (1.7) Multiple Sequence Alignments

```
Sequence format is Pearson
Sequence 1: 1600202CD1          129 aa
Sequence 2: ND5-I__21-35_        15 aa
Start of Pairwise alignments
Aligning...
Sequences (1:2) Aligned. Score:  26
Start of Multiple Alignment
There are 1 groups
Aligning...
Group 1:                     Delayed
Sequence:1     Score:0
Sequence:2     Score:116
Alignment Score -2
CLUSTAL-Alignment file created  [baaUeaWmW.aln]
CLUSTAL W (1.7) multiple sequence alignment


1600202CD1          MSFPKYKPSSLRTLPETLDPAEYNISPETRRAQAERLAIRAQLKREYLLQYNDPNRRGLI
ND5-I__21-35_       --------------TTLVNPNKKNSYPHY-------------------------------
                                  .  ::* : *  *.

1600202CD1          ENPALLRWAYARTINVYPNFRPTPKNSLMGALCGFGPLIFIYYIIKTERDRKEKLIQEGK
ND5-I__21-35_       ------------------------------------------------------------


1600202CD1          LDRTFHLSY
ND5-I__21-35_       ---------
```

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ClustalW Results

Sequences | Help

Retrieval | BLAST2 | FASTA | ClustalW | GCG Assembly | Phrap | Translation

 SeqServer Version 4.6 Jan 2002

- ☐ 1600202CD1
- ☐ ND6-I3_(128-144)

CLUSTAL W (1.7) Multiple Sequence Alignments

```
Sequence format is Pearson
Sequence 1: 1600202CD1            129 aa
Sequence 2: ND6-I3__128-144_       19 aa
Start of Pairwise alignments
Aligning...
Sequences (1:2) Aligned. Score:  15
Start of Multiple Alignment
There are 1 groups
Aligning...
Group 1:                    Delayed
Sequence:1     Score:0
Sequence:2     Score:119
Alignment Score -13
CLUSTAL-Alignment file created  [baaw2aypW.aln]
CLUSTAL W (1.7) multiple sequence alignment


1600202CD1            MSFPKYKPSSLRTLPETLDPAEYNISPETRRAQAERLAIRAQLKREYLLQYNDPNRRGLI
ND6-I3__128-144_      ----------------------------------------------------EGEGSGSGFI
                                                                          .: .  *:*

1600202CD1            ENPALLRWAYARTINVYPNFRPTPKNSLMGALCGFGPLIFIYYIIKTERDRKEKLIQEGK
ND6-I3__128-144_      REDPIGAGA-----------------------------------------------------
                      .: .:   *

1600202CD1            LDRTFHLSY
ND6-I3__128-144_      ---------
```

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